REMARKS

Claims 1-10, 12-24 and 27-33 are pending in the application. Claims 3-5, 7, 8, 10, 16, 19, 20, 23, 24, and 29 are withdrawn from consideration. Applicants reiterate their previous arguments and provide additional evidence and argument traversing the rejections as follows.

Request for Telephonic Interview

Applicants formally request a telephonic interview prior to examination. The undersigned may be reached at (858) 228-7829.

Objections to the Specification

The specification was objected to on the bases that pages 18, 24 and 25 of the application allegedly recited trademarked information without accompanying generic language. In each instance, a list of items was introduced with accompanying generic language applying to each item in the list. A careful review of the CFR and MPEP, along with conversations with USPTO personnel, indicate that this is sufficient. Nevertheless, in order to expedite prosecution, the specification has been amended above to recite further iterations of generic language with each trademarked item in the respective lists. Withdrawal of the objection is respectfully requested.

35 U.S.C. § 112

Claims 1, 2, 6, 9, 12-15, 17-18, 21, 22, 27, 28 and 30-33 were rejected under 35 U.S.C. 112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "polynucleotide binding protein" was asserted to be indefinite and "non-limiting" and "cannot be readily determined." The claims were also alleged to be indefinite "as it is not readily apparent just what the claimed method is to result in."

The standard for establishing the definiteness of a claim requires simply that a person of skill in the art can discern the meaning of the claim or claim term.

"Polynucleotide binding protein." The application at pages 22 and 23 describes "a sensor PBP [polynucleotide binding protein] … that binds to the target polynucleotide to be

assayed," and further recites that "[a]ny protein which can bind to a target polynucleotide of interest can be employed in the methods disclosed."

Further, the plain language of the claims requires the PBP to have the ability to bind a corresponding target. Claim 1 (and 33) recites that the polynucleotide binding protein (PBP) "can bind to the target polynucleotide" and that the sample is contacted "under conditions in which the sensor PBP can (preferentially) bind to the target polynucleotide, if present."

The Office Action interprets the allegedly indefinite phrase as covering "any protein under the sun that can bind a polynucleotide, be it directly or indirectly, and also includes those proteins of unknown binding specificity." Office Action at 5. This includes at least the phrases "under the sun" and "directly or indirectly" that do not appear in the claims or the specification.

To the extent that the Office Action relies on descriptions of embodiments in the specification not falling within the claim scope, such reliance is contrary to law and improper:

> Limitations appearing in the specification but not recited in the claim should not be read into the claim. *E-Pass Techs., Inc. v. 3Com Corp.*, 343 F.3d 1364, 1369, 67 USPQ2d 1947, 1950 (Fed. Cir. 2003) (claims must be interpreted "in view of the specification" without importing limitations from the specification into the claims unnecessarily). *In re Prater*, 415 F.2d 1393, 1404-05, 162 USPQ 541, 550-551 (CCPA 1969).

MPEP 2106. The claims plainly recite that the sensor PBP can bind to the target polynucleotide, and thus embodiments involving screening methods described in the application utilizing candidate binding proteins do not fall within the claim scope.

Applicants herein provide the declaration of one of skill in the art who can discern the meaning of this claim term. Attached is the declaration of Kieran Elborough, D.Phil., an experienced scientist with knowledge of the art, who has performed experiments utilizing polynucleotide binding proteins and published corresponding results in peer-reviewed journals. Dr. Elborough has reviewed the application and claims as well as the Office Action. Dr. Elborough is able to discern the meaning of this claim term.

As the indefiniteness rejection is based on an improper importation of limitations from

the specification into the claims, the rejection is improper. The declaration of Dr. Elborough demonstrates that one of skill can interpret this claim term based on the teachings in the application. No admissible evidence has been provided that a person of skill is not able to discern the meaning of this claim term. Withdrawal of the rejection is respectfully requested.

"What the claimed method is to result in." The Office Action asserted that the claimed assay resulted in light detection and that it was "not readily apparent just what the claimed method is to result in."

As previously stated, this stated grounds does not meet the standard for establishing indefiniteness.

Nevertheless, in order to expedite prosecution, the claims have been amended to more explicitly clarify the nature of the claimed invention, which involves energy transfer upon binding of a labeled sensor PBP to its respective target polynucleotide. The target polynucleotide associates with a polycationic multichromophore that can transfer energy upon binding to a signaling chromophore conjugated to the sensor PBP. The energy transfer obtained when the multichromophore is excited only occurs when the signaling chromophore is brought into proximity by the binding of sensor to target. The light detected is specific for the signaling chromophore, indicating such binding.

The attached declaration of Dr. Elborough further states that he has reviewed the application and fully understands the meaning of the claimed method.

The claim amendments are believed to clarify the claims and thus obviate this stated rejection. The declaration of Dr. Elborough further establishes that one of skill can interpret the meaning of the claimed method in light of the teachings in the application. No admissible evidence has been provided that a person of skill is not able to discern the meaning of this claim term. Withdrawal of the rejection is respectfully requested.

The enablement rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 2, 6, 9, 12-15, 17, 22, 27, 28 and 30-32 were rejected under 35 U.S.C. 112, first paragraph, as allegedly lacking enablement. This rejection is traversed.

WORKING EXAMPLES AND A CLAIMED GENUS

> For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.

MPEP 2164.02

Here, working examples of the claimed invention have been provided along with accompanying generic language. No reasons whatsoever have been offered by the examiner as to why a person skilled in the art could not use the genus as claimed.

In addition to those previously stated, the following arguments and evidence are provided in support of the enablement of the invention.

Quantity of experimentation. The Office Action asserts, without support or any stated factual basis, that the quantity of experimentation would be several man-years. No evidence was provided how or why this amount of experimentation would be necessary.

The attached declaration of the inventor Guillermo C. Bazan establishes that the amount of experimentation actually undertaken in reducing the invention to practice was no more than approximately three months. Materials used in performance of the experiments presented in the application were ordered on or about June 10, 2002. A working embodiment of the invention was reduced to practice on or about September 13, 2002. This amount of experimentation is in no way undue, and in fact represents remarkable rapidity.

Working Examples. The Office Action concedes that seven working examples are provided, but provides specious asserted grounds for discounting the value of these examples. Such examples are entitled to substantial weight.

As well-established, a patent applicant is not required to teach that which is well known in the art:

> A patent specification need not teach, and preferably omits, what is well known in the art. *Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, 231 USPQ 81, 94 (Fed. Cir. 1986).

MPEP 2182.

The Office Action's assertions that a person of skill would not know how to synthesize a peptide that is (a) known in the art and (b) whose sequence is actually presented in the application are respectfully not made in good faith. The Office Action is in fact asserting that persons of skill in the biotechnological arts cannot make a protein. Clearly, this is not the case.

The Office Action's further assertions that the person of skill would not know how to produce and use the elected fluorescent dye are similarly without basis. Attached hereto and hereby incorporated is a copy of the Merck Manual from 1983, describing the structure of the elected dye fluorescein and citing its synthesis by Fisher in 1922. Furthermore, the 1997 publication of Lohse et al. (Bioconjugate Chem. 8:503-509) has previously been provided in an Information Disclosure Statement describing the use of fluorescein ethyl ester for incorporation into lysine monomers and oligomers and peptides. Thus, it was known in the art at the time of invention how to make fluorescein and use it to label peptides.

The working examples thus provide substantial evidence of enablement. The assertions that the techniques presented in the application were not known in the art are without foundation, and are further contradicted by the evidence provided above.

The nature of the invention and the predictability of the art. The Office Action blatantly mischaracterizes the invention as allegedly employing non-specific binding of nucleic acids. The invention provides for a variety of embodiments utilizing polynucleotide-binding proteins of varying specificities. Claim 33 further explicitly recites that the binding be preferential.

The interpretation of this factor is further improper in that the Office Action relies on an improper interpretation of the term "polynucleotide binding protein." For the reasons set forth above, this term can be discerned by a person of skill in the art. The attached declaration of Dr. Kieran Elborough provides evidentiary support that the term is definite and that the person of skill understands how to perform the claimed invention from the application's teachings.

Breadth of the invention. The Office Action provides the strained assertion that the possibility of false positives therefore renders the claimed method without enablement. This is without merit. In addition to the teachings in the application, one of skill in the art has knowledge of how to perform control experiments and how to distinguish and correct for conditions in differing experimental formats. The working embodiments in fact provide evidence of exactly how to perform control experiments, utilizing sequences of altered sequence in order to prove that the claimed methods provide exquisite selectivity in the exemplified format.

That the invention can be used in other formats utilizing binding proteins of differing binding specificity is in fact evidence of the utility of the invention, and in no way discounts the enablement of the claimed invention.

Further publications exemplifying the utility and knowledge in the art of the value of various detection methods for RNA and DNA are described below. The Office Action asserted that the dates of the prior-provided materials as later than that of the application priority date rendered such materials as inadmissible, without actually addressing the merits of the arguments that such methods have long been used in the art. The materials provided herein have been selected from those available prior to the priority date, thereby rendering this objection to the prior-provided evidence moot.

For the grounds previously stated, as well as the arguments herein, the enablement rejection lacks support. Withdrawal is respectfully requested.

The rejection under 35 U.S.C. §101

Claims 1, 2, 6, 9, 12-15, 17-18, 21-22, 27, 28 and 30-33 were rejected under 35 U.S.C. 101 as allegedly not supported by either a specific, substantial, and credible asserted utility or a well established utility. This rejection is traversed.

As explained at MPEP 2107.01:

> Some confusion can result when one attempts to label certain types of inventions as not being capable of having a specific and substantial utility based on the setting in which the invention is to be used. One example is inventions to be used in a research or laboratory setting. Many research tools such as gas chromatographs, screening assays,

and nucleotide sequencing techniques have a clear, specific and unquestionable utility (e.g., they are useful in analyzing compounds).

A method of detecting and/or quantitating nucleic acids is useful in analyzing compounds (i.e., nucleic acids). Thus, the invention as claimed has a clear, specific and unquestionable utility.

The Office Action asserts that, because a particular nucleotide being detected might have an unknown utility, the claimed method therefore lacks utility. This strained argument lacks merit. A nucleotide sequencing technique could similarly be used to sequence a nucleotide of unknown utility. Following the argument of the Office Action, all nucleotide sequencing technique would therefore lack utility. Plainly, that is not the case. Nucleotide sequencing techniques, like nucleotide detection and quantitation techniques, have clear, specific and unquestionable utility.

The attached materials provide evidence of the known utility of methods of detecting and/or quantitating RNA and DNA, prior to the priority date of the instant application. Such methods have established commercial markets demonstrating their utility to persons of skill. The attached materials include:

(1) A 1977 publication by Latt demonstrating the utility of Hoechst 33258 in fluorometric detection of DNA synthesis, describing the utility of optical methods for studying DNA synthesis;

(2) A 1987 by Mocharla et al. demonstrating the utility of a method for detecting DNA in RNA preparations utilizing Hoechst 33258 with high sensitivity;

(3) A 2000 (see copyright at page 8) Molecular Probes catalog presenting various RNA and DNA stains commercially available and used for detection and quantitation of RNA and DNA, including SYBR Green I, SYBR Green II and SYBR Gold nucleic acid stains, PicoGreen dsDNA quantitation agent, RiboGreen RNA quantitation agent, and OliGreen ssDNA quantitation agent.

Thus, methods of detecting and/or quantitating nucleic acids had well-established utilities prior to the application priority date.

To the extent that the rejection is based on an asserted inability to understand the claimed method, the clarifying amendments are asserted to obviate and overcome the asserted rejection.

For the reasons set forth in this and prior responses, withdrawal of the rejection is respectfully requested.

The "how to use" rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 2, 6, 9, 12-15, 17-18, 21-22, 27, 28 and 30-33 were rejected under 35 U.S.C. 112, first paragraph, on the ground that one of skill would allegedly not know how to use the invention. This rejection is traversed.

To the extent that the rejection is based on an asserted inability to understand the claimed method, the clarifying amendments are asserted to obviate and overcome the asserted rejection.

Further, the accompanying declaration of Kieran Elborough establishes that a person of skill in the art understands the full scope of claim 1, and therefore understands how to use the invention.

For the reasons set forth in this and prior responses, withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicants respectfully submit that the claims are in condition for allowance, and a corresponding notice of allowance is respectfully requested. A telephonic interview is formally requested prior to examination after entry of the accompanying Request for Continued Examination.

Respectfully submitted,
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ATTACHMENTS